

1 1. A DNA construct that alters expression of an
2 endogenous G-CSF gene in a mammalian cell upon integration
3 into the genome of the cell via homologous recombination,
4 the construct comprising: (i) a targeting sequence
5 containing at least 20 contiguous nucleotides from
6 SEQ ID NO:5 and (ii) a transcriptional regulatory sequence.

1 2. The DNA construct of claim 1, wherein the
2 construct further comprises an exon and a splice-donor site.

1 3. The DNA construct of claim 2, wherein the
2 construct further comprises, downstream from the splice-
3 donor site, an intron and a splice-acceptor site.

1 4. The DNA construct of claim 1, wherein the
2 construct further comprises a selectable marker gene.

1 5. The DNA construct of claim 1, wherein the
2 targeting sequence contains at least 50 contiguous
3 nucleotides from SEQ ID NO:5.

1 6. An isolated nucleic acid comprising at least 20
2 contiguous nucleotides of SEQ ID NO:5 or its complement,
3 wherein the isolated nucleic acid does not encode full-
4 length G-CSF.

1 7. The isolated nucleic acid of claim 6, wherein
2 the isolated nucleic acid comprises at least 50 contiguous
3 nucleotides of SEQ ID NO:5 or its complement.

1 8. The isolated nucleic acid of claim 6, wherein
2 the isolated nucleic acid comprises at least 100 contiguous
3 nucleotides of SEQ ID NO:5 or its complement.

1 9. The isolated nucleic acid of claim 6, wherein
2 the isolated nucleic acid comprises at least 200 contiguous
3 nucleotides of SEQ ID NO:5 or its complement.

1 10. The isolated nucleic acid of claim 6, wherein
2 the isolated nucleic acid comprises at least 500 contiguous
3 nucleotides of SEQ ID NO:5 or its complement.

1 11. The isolated DNA of claim 6, wherein the
2 isolated nucleic acid comprises nucleotides 1470 to 4723 of
3 SEQ ID NO:5, or its complement.

1 12. The isolated DNA of claim 6, wherein the
2 isolated nucleic acid comprises SEQ ID NO:5 or its
3 complement.

1 13. An isolated nucleic acid comprising a strand
2 that comprises a nucleotide sequence that (i) is at least
3 100 nucleotides in length and (ii) hybridizes under highly
4 stringent conditions with SEQ ID NO:5 or the complement
5 thereof.

1 14. The isolated nucleic acid of claim 13, wherein
2 the nucleotide sequence is at least 200 nucleotides in
3 length.

1 15. The isolated nucleic acid of claim 13, wherein
2 the nucleotide sequence is at least 400 nucleotides in
3 length.

1 16. The isolated nucleic acid of claim 13, wherein
2 the nucleotide sequence is at least 1,000 nucleotides in
3 length.

1 17. An isolated nucleic acid comprising a strand
2 that comprises a nucleotide sequence that (i) is at least
3 100 nucleotides in length and (ii) shares at least 80%
4 sequence identity with a fragment of SEQ ID NO:5 having the
5 same length as the nucleotide sequence.

1 18. The isolated nucleic acid of claim 17, wherein
2 the nucleotide sequence is at least 200 nucleotides in
3 length.

1 19. The isolated nucleic acid of claim 18, wherein
2 the nucleotide sequence is at least 400 nucleotides in
3 length.

1 20. The isolated nucleic acid of claim 18, wherein
2 the nucleotide sequence is at least 1,000 nucleotides in
3 length.

1 21. A homologously recombinant cell stably
2 transfected with the DNA construct of claim 1, the DNA
3 construct having undergone homologous recombination with
4 genomic DNA upstream of the ATG initiation codon of an
5 endogenous G-CSF coding sequence.

1 22. A homologously recombinant cell stably
2 transfected with the DNA construct of claim 2, the DNA
3 construct having undergone homologous recombination with
4 genomic DNA upstream of the ATG initiation codon of an
5 endogenous G-CSF coding sequence.

1 23. A homologously recombinant cell stably
2 transfected with the DNA construct of claim 3, the DNA
3 construct having undergone homologous recombination with
4 genomic DNA upstream of the ATG initiation codon of an
5 endogenous G-CSF coding sequence.

1 24. A homologously recombinant cell stably
2 transfected with the DNA construct of claim 4, the DNA
3 construct having undergone homologous recombination with
4 genomic DNA upstream of the ATG initiation codon of an
5 endogenous G-CSF coding sequence.

1 25. A method of altering expression of an
2 endogenous G-CSF gene in a mammalian cell, the method
3 comprising
4 introducing the DNA construct of claim 1 into the
5 cell;
6 maintaining the cell under conditions which permit
7 homologous recombination to occur between the construct and
8 a genomic target site homologous to the targeting sequence,
9 to produce a homologously recombinant cell; and
10 maintaining the homologously recombinant cell under
11 conditions which permit expression of the G-CSF coding
12 sequence under the control of the transcriptional regulatory
13 sequence.

1 26. A method of altering expression of an
2 endogenous G-CSF gene in a mammalian cell, the method
3 comprising
4 introducing the DNA construct of claim 4 into the
5 cell;
6 maintaining the cell under conditions which permit
7 homologous recombination to occur between the construct and
8 a genomic target site homologous to the targeting sequence,
9 to produce a homologously recombinant cell; and
10 maintaining the homologously recombinant cell under
11 conditions which permit expression of the G-CSF coding
12 sequence under the control of the transcriptional regulatory
13 sequence.

1 27. A method of delivering G-CSF to an animal,
2 comprising
3 providing the cell of claim 21, and
4 implanting the cell in the animal, wherein the cell
5 secretes G-CSF.

1 28. A method of delivering G-CSF to an animal,
2 comprising
3 providing the cell of claim 22, and
4 implanting the cell in the animal, wherein the cell
5 secretes G-CSF.

1 29. A method of delivering G-CSF to an animal,
2 comprising
3 providing the cell of claim 23, and
4 implanting the cell in the animal, wherein the cell
5 secretes G-CSF.

1 30. A method of delivering G-CSF to an animal,
2 comprising
3 providing the cell of claim 24, and
4 implanting the cell in the animal, wherein the cell
5 secretes G-CSF.

1 31. A method of producing G-CSF, comprising
2 providing the cell of claim 21, and
3 culturing the cell *in vitro* under conditions which
4 permit the cell to express and secrete G-CSF.

1 32. A method of producing G-CSF, comprising
2 providing the cell of claim 22, and
3 culturing the cell *in vitro* under conditions which
4 permit the cell to express and secrete G-CSF.

1 33. A method of producing G-CSF, comprising
2 providing the cell of claim 23, and
3 culturing the cell *in vitro* under conditions which
4 permit the cell to express and secrete G-CSF.

1 34. A method of producing G-CSF, comprising
2 providing the cell of claim 24, and
3 culturing the cell *in vitro* under conditions which
4 permit the cell to express and secrete G-CSF.

Add 03